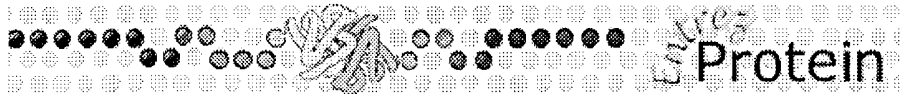

☐ **1:** P22607. Fibroblast growth...[gi:120050] BLink, Domains, Links

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DEFINITION  Fibroblast growth factor receptor 3 precursor (FGFR-3).
ACCESSION   P22607
VERSION     P22607  GI:120050
DBSOURCE    swissprot: locus FGR3_HUMAN, accession P22607;
            class: standard.
            extra accessions:Q14308,Q16294,Q16608,created: Aug 1, 1991.
            sequence updated: Aug 1, 1991.
            annotation updated: Oct 1, 2004.
            xrefs: gi: 182568, gi: 182569, gi: 7533124, gi: 7533125, gi:
            182564, gi: 182565, gi: 186622, gi: 186623, gi: 914201, gi: 914202,
            gi: 695548, gi: 695549, gi: 841313, gi: 841314, gi: 476557, pdb
            accession 1RY7
            xrefs (non-sequence databases): IntActP22607, GenewHGNC:3690, MIM
            134934, MIM 100800, MIM 123500, MIM 146000, MIM 187600, MIM 187601,
            MIM 600593, MIM 109800, MIM 603956, GO0005887, GO0005007,
            GO0016049, GO0008543, GO0007259, GO0000165, GO0001501,
            InterProIPR007110, InterProIPR011009, InterProIPR000719,
            InterProIPR001245, InterProIPR008266, PfamPF00047, PfamPF00069,
            PRINTSPR00109, ProDomPD000001, PROSITEPS50835, PROSITEPS00107,
            PROSITEPS50011, PROSITEPS00109
KEYWORDS    3D-structure; Alternative splicing; ATP-binding; Chromosomal
            translocation; Disease mutation; Dwarfism; Glycoprotein;
            Immunoglobulin domain; Phosphorylation; Receptor; Repeat; Signal;
            Transferase; Transmembrane; Tyrosine-protein kinase.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 806)
  AUTHORS   Keegan,K., Johnson,D.E., Williams,L.T. and Hayman,M.J.
  TITLE     Isolation of an additional member of the fibroblast growth factor
            receptor family, FGFR-3
  JOURNAL   Proc. Natl. Acad. Sci. U.S.A. 88 (4), 1095-1099 (1991)
  MEDLINE   91142118
   PUBMED   1847508
  REMARK    SEQUENCE FROM N.A. (ISOFORM 1).
REFERENCE   2  (residues 1 to 806)
  AUTHORS   Terada,M., Shimizu,A. and Seo,M.
  TITLE     Direct Submission
  JOURNAL   Submitted (??-MAR-2000)
  REMARK    SEQUENCE FROM N.A. (ISOFORM 3).
REFERENCE   3  (residues 1 to 806)
  AUTHORS   Thompson,L.M., Plummer,S., Schalling,M., Altherr,M.R.,
            Gusella,J.F., Housman,D.E. and Wasmuth,J.J.
  TITLE     A gene encoding a fibroblast growth factor receptor isolated from
            the Huntington disease gene region of human chromosome 4
  JOURNAL   Genomics 11 (4), 1133-1142 (1991)
  MEDLINE   92147110
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PUBMED 1664411
REMARK SEQUENCE OF 76-806 FROM N.A. (ISOFORM 1), AND TISSUE SPECIFICITY. TISSUE=Fetal brain
REFERENCE 4 (residues 1 to 806)
AUTHORS Partanen,J., Makela,T.P., Alitalo,R., Lehvaslaiho,H. and Alitalo,K.
TITLE Putative tyrosine kinases expressed in K-562 human leukemia cells
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 87 (22), 8913-8917 (1990)
MEDLINE 91062389
PUBMED 2247464
REMARK SEQUENCE OF 614-681 FROM N.A.
REFERENCE 5 (residues 1 to 806)
AUTHORS Murgue,B., Tsunekawa,S., Rosenberg,I., deBeaumont,M. and Podolsky,D.K.
TITLE Identification of a novel variant form of fibroblast growth factor receptor 3 (FGFR3 IIIb) in human colonic epithelium
JOURNAL Cancer Res. 54 (19), 5206-5211 (1994)
MEDLINE 95007529
PUBMED 7923141
REMARK SEQUENCE OF 311-358 FROM N.A. (ISOFORM 2). TISSUE=Colon tumor
REFERENCE 6 (residues 1 to 806)
AUTHORS Scotet,E. and Houssaint,E.
TITLE The choice between alternative IIIb and IIIc exons of the FGFR-3 gene is not strictly tissue-specific
JOURNAL Biochim. Biophys. Acta 1264 (2), 238-242 (1995)
MEDLINE 96085129
PUBMED 7495869
REMARK SEQUENCE OF 311-358 FROM N.A. (ISOFORM 2). TISSUE=Keratinocytes
REFERENCE 7 (residues 1 to 806)
AUTHORS Rousseau,F., Bonaventure,J., Legeai-Mallet,L., Pelet,A., Rozet,J.M., Maroteaux,P., Le Merrer,M. and Munnich,A.
TITLE Mutations in the gene encoding fibroblast growth factor receptor-3 in achondroplasia
JOURNAL Nature 371 (6494), 252-254 (1994)
MEDLINE 94359611
PUBMED 8078586
REMARK VARIANT ACH ARG-380.
REFERENCE 8 (residues 1 to 806)
AUTHORS Bellus,G.A., Hefferon,T.W., Ortiz de Luna,R.I., Hecht,J.T., Horton,W.A., Machado,M., Kaitila,I., McIntosh,I. and Francomano,C.A.
TITLE Achondroplasia is defined by recurrent G380R mutations of FGFR3
JOURNAL Am. J. Hum. Genet. 56 (2), 368-373 (1995)
MEDLINE 95150025
PUBMED 7847369
REMARK VARIANT ACH ARG-380.
REFERENCE 9 (residues 1 to 806)
AUTHORS Superti-Furga,A., Eich,G., Bucher,H.U., Wisser,J., Giedion,A., Gitzelmann,R. and Steinmann,B.
TITLE A glycine 375-to-cysteine substitution in the transmembrane domain of the fibroblast growth factor receptor-3 in a newborn with achondroplasia
JOURNAL Eur. J. Pediatr. 154 (3), 215-219 (1995)
MEDLINE 95278277
PUBMED 7758520
REMARK VARIANT ACH CYS-375.
REFERENCE 10 (residues 1 to 806)
AUTHORS Tavormina,P.L., Rimoin,D.L., Cohn,D.H., Zhu,Y.Z., Shiang,R. and Wasmuth,J.J.

TITLE Another mutation that results in the substitution of an unpaired cysteine residue in the extracellular domain of FGFR3 in thanatophoric dysplasia type I
JOURNAL Hum. Mol. Genet. 4 (11), 2175-2177 (1995)
MEDLINE 96154693
PUBMED 8589699
REMARK VARIANT TD1 CYS-249.
REFERENCE 11 (residues 1 to 806)
AUTHORS Tavormina,P.L., Shiang,R., Thompson,L.M., Zhu,Y.Z., Wilkin,D.J., Lachman,R.S., Wilcox,W.R., Rimoin,D.L., Cohn,D.H. and Wasmuth,J.J.
TITLE Thanatophoric dysplasia (types I and II) caused by distinct mutations in fibroblast growth factor receptor 3
JOURNAL Nat. Genet. 9 (3), 321-328 (1995)
MEDLINE 95291326
PUBMED 7773297
REMARK VARIANTS TD1 CYS-248 AND CYS-371, AND VARIANT TD2 GLU-650.
REFERENCE 12 (residues 1 to 806)
AUTHORS Bellus,G.A., McIntosh,I., Smith,E.A., Aylsworth,A.S., Kaitila,I., Horton,W.A., Greenhaw,G.A., Hecht,J.T. and Francomano,C.A.
TITLE A recurrent mutation in the tyrosine kinase domain of fibroblast growth factor receptor 3 causes hypochondroplasia
JOURNAL Nat. Genet. 10 (3), 357-359 (1995)
MEDLINE 95400307
PUBMED 7670477
REMARK VARIANT HYPOCHONDROPLASIA LYS-540.
REFERENCE 13 (residues 1 to 806)
AUTHORS Meyers,G.A., Orlow,S.J., Munro,I.R., Przylepa,K.A. and Jabs,E.W.
TITLE Fibroblast growth factor receptor 3 (FGFR3) transmembrane mutation in Crouzon syndrome with acanthosis nigricans
JOURNAL Nat. Genet. 11 (4), 462-464 (1995)
MEDLINE 96083601
PUBMED 7493034
REMARK VARIANT CROUZON GLU-391.
REFERENCE 14 (residues 1 to 806)
AUTHORS Webster,M.K. and Donoghue,D.J.
TITLE Constitutive activation of fibroblast growth factor receptor 3 by the transmembrane domain point mutation found in achondroplasia
JOURNAL EMBO J. 15 (3), 520-527 (1996)
MEDLINE 96174812
PUBMED 8599935
REMARK CHARACTERIZATION OF VARIANT ACH ARG-380.
REFERENCE 15 (residues 1 to 806)
AUTHORS Rousseau,F., el Ghouzzi,V., Delezoide,A.L., Legeai-Mallet,L., Le Merrer,M., Munnich,A. and Bonaventure,J.
TITLE Missense FGFR3 mutations create cysteine residues in thanatophoric dwarfism type I (TD1)
JOURNAL Hum. Mol. Genet. 5 (4), 509-512 (1996)
MEDLINE 96254981
PUBMED 8845844
REMARK VARIANTS TD1 CYS-248; CYS-249; CYS-370 AND CYS-373.
REFERENCE 16 (residues 1 to 806)
AUTHORS Muenke,M., Gripp,K.W., McDonald-Mcginn,D.M., Gaudenz,K., Whitaker,L.A., Bartlett,S.P., Markowitz,R.I., Robin,N.H., Nwokoro,N., Mulvihill,J.J., Losken,H.W., Mulliken,J.B., Guttmacher,A.E., Wilroy,R.S., Clarke,L.A., Hollway,G., Ades,L.C., Haan,E.A., Mulley,J.C., Cohen,M.M.Jr., Bellus,G.A., Francomano,C.A., Moloney,D.M., Wall,S.A., Wilkie,A.O.M. and Zackai,E.H.
TITLE A unique point mutation in the fibroblast growth factor receptor 3 gene (FGFR3) defines a new craniosynostosis syndrome

JOURNAL Am. J. Hum. Genet. 60 (3), 555-564 (1997)
MEDLINE 97195541
PUBMED 9042914
REMARK VARIANT CRS3 ARG-250.
REFERENCE 17 (residues 1 to 806)
AUTHORS Katsumata,N., Kuno,T., Miyazaki,S., Mikami,S., Nagashima-Miyokawa,A., Nimura,A., Horikawa,R. and Tanaka,T.
TITLE G370C mutation in the FGFR3 gene in a Japanese patient with thanatophoric dysplasia
JOURNAL Endocr. J. 45 Suppl, S171-S174 (1998)
MEDLINE 99004917
PUBMED 9790257
REMARK VARIANT TD1 CYS-370.
REFERENCE 18 (residues 1 to 806)
AUTHORS Grigelioniene,G., Hagenas,L., Eklof,O., Neumeyer,L., Haereid,P.E. and Anvret,M.
TITLE A novel missense mutation Ile538Val in the fibroblast growth factor receptor 3 in hypochondroplasia. Mutations in brief no. 122. Online
JOURNAL Hum. Mutat. 11 (4), 333 (1998)
MEDLINE 99229535
PUBMED 10215410
REMARK VARIANT HYPOCHONDROPLASIA VAL-538.
REFERENCE 19 (residues 1 to 806)
AUTHORS Deutz-Terlouw,P.P., Losekoot,M., Aalfs,C.M., Hennekam,R.C. and Bakker,E.
TITLE Asn540Thr substitution in the fibroblast growth factor receptor 3 tyrosine kinase domain causing hypochondroplasia
JOURNAL Hum. Mutat. Suppl 1, S62-S65 (1998)
PUBMED 9452043
REMARK VARIANT HYPOCHONDROPLASIA THR-540.
REFERENCE 20 (residues 1 to 806)
AUTHORS Kitoh,H., Brodie,S.G., Kupke,K.G., Lachman,R.S. and Wilcox,W.R.
TITLE Lys650Met substitution in the tyrosine kinase domain of the fibroblast growth factor receptor gene causes thanatophoric dysplasia Type I. Mutations in brief no. 199. Online
JOURNAL Hum. Mutat. 12 (5), 362-363 (1998)
MEDLINE 20133862
PUBMED 10671061
REMARK VARIANT TD1 MET-650.
REFERENCE 21 (residues 1 to 806)
AUTHORS Cappellen,D., De Oliveira,C., Ricol,D., de Medina,S., Bourdin,J., Sastre-Garau,X., Chopin,D., Thiery,J.P. and Radvanyi,F.
TITLE Frequent activating mutations of FGFR3 in human bladder and cervix carcinomas
JOURNAL Nat. Genet. 23 (1), 18-20 (1999)
MEDLINE 99400545
PUBMED 10471491
REMARK VARIANTS BLADDER AND CERVIX CANCERS CYS-248; CYS-249; CYS-370 AND GLU-650.
REFERENCE 22 (residues 1 to 806)
AUTHORS Bellus,G.A., Spector,E.B., Speiser,P.W., Weaver,C.A., Garber,A.T., Bryke,C.R., Israel,J., Rosengren,S.S., Webster,M.K., Donoghue,D.J. and Francomano,C.A.
TITLE Distinct missense mutations of the FGFR3 lys650 codon modulate receptor kinase activation and the severity of the skeletal dysplasia phenotype
JOURNAL Am. J. Hum. Genet. 67 (6), 1411-1421 (2000)
MEDLINE 20530223
PUBMED 11055896
REMARK VARIANT HYPOCHONDROPLASIA GLN-650.

REFERENCE 23 (residues 1 to 806)
AUTHORS Mortier,G., Nuytinck,L., Craen,M., Renard,J.P., Leroy,J.G. and de Paepe,A.
TITLE Clinical and radiographic features of a family with hypochondroplasia owing to a novel Asn540Ser mutation in the fibroblast growth factor receptor 3 gene
JOURNAL J. Med. Genet. 37 (3), 220-224 (2000)
MEDLINE 20236347
PUBMED 10777366
REMARK VARIANT HYPOCHONDROPLASIA SER-540.
REFERENCE 24 (residues 1 to 806)
AUTHORS Jang,J.H., Shin,K.H. and Park,J.G.
TITLE Mutations in fibroblast growth factor receptor 2 and fibroblast growth factor receptor 3 genes associated with human gastric and colorectal cancers
JOURNAL Cancer Res. 61 (9), 3541-3543 (2001)
MEDLINE 21225299
PUBMED 11325814
REMARK VARIANT COLORECTAL CANCER LYS-322.
REFERENCE 25 (residues 1 to 806)
AUTHORS Sibley,K., Cuthbert-Heavens,D. and Knowles,M.A.
TITLE Loss of heterozygosity at 4p16.3 and mutation of FGFR3 in transitional cell carcinoma
JOURNAL Oncogene 20 (6), 686-691 (2001)
MEDLINE 21214464
PUBMED 11314002
REMARK VARIANT BLADDER CANCER GLN-650.
REFERENCE 26 (residues 1 to 806)
AUTHORS Thauvin-Robinet,C., Faivre,L., Lewin,P., De Monleon,J.V., Francois,C., Huet,F., Couailler,J.F., Campos-Xavier,A.B., Bonaventure,J. and Le Merrer,M.
TITLE Hypochondroplasia and stature within normal limits: another family with an Asn540Ser mutation in the fibroblast growth factor receptor 3 gene
JOURNAL Am. J. Med. Genet. 119A (1), 81-84 (2003)
MEDLINE 22591861
PUBMED 12707965
REMARK VARIANT HYPOCHONDROPLASIA SER-540.
COMMENT ----------
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The original entry is available from http://www.expasy.ch/sprot and http://www.ebi.ac.uk/sprot
----------.
[FUNCTION] Receptor for acidic and basic fibroblast growth factors. Preferentially binds FGF1.
[CATALYTIC ACTIVITY] ATP + a protein tyrosine = ADP + protein tyrosine phosphate.
[SUBCELLULAR LOCATION] Type I membrane protein.
[ALTERNATIVE PRODUCTS] Event=Alternative splicing; Named isoforms=3; Name=1; Synonyms=IIIc; IsoId=P22607-1; Sequence=Displayed; Name=2; Synonyms=IIIb; IsoId=P22607-2; Sequence=VSP_002988; Name=3; IsoId=P22607-3; Sequence=VSP_002989.
[TISSUE SPECIFICITY] Expressed in brain, kidney and testis. Very low or no expression in spleen, heart, and muscle. In 20- to 22-week old fetuses it is expressed at high level in kidney, lung, small intestine and brain, and to a lower degree in spleen, liver, and muscle. Epithelial cells show exclusively isoform 2 transcripts while fibroblastic cells show a mixture of isoforms 1 and 2

transcripts.
[DISEASE] Defects in FGFR3 are the cause of achondroplasia (ACH) [MIM:100800]. ACH is an autosomal dominant disease and is the most frequent form of short-limb dwarfism. It is characterized by a long, narrow trunk, short extremities, particularly in the proximal (rhizomelic) segments, a large head with frontal bossing, hypoplasia of the midface and a trident configuration of the hands.
[DISEASE] Defects in FGFR3 are a cause of Crouzon syndrome [MIM:123500]; also called craniofacial dysostosis type I (CFD1). Crouzon syndrome is characterized by craniosynostosis (premature fusion of the skull sutures), hypertelorism, exophthalmos and external strabismus, parrot-beaked nose, short upper lip, hypoplastic maxilla, and a relative mandibular prognathism.
[DISEASE] Defects in FGFR3 are a cause of thanatophoric dysplasia (TD) [MIM:187600, 187601]; also known as thanatophoric dwarfism. TD is the most common neonatal lethal skeletal dysplasia. Affected individuals display features similar to those seen in homozygous achondroplasia. It causes severe shortening of the limbs with macrocephaly, narrow thorax and short ribs. In the most common subtype, TD1 [MIM:187600], femur are curved, while in TD2 [MIM:187601], straight femurs are associated with cloverleaf skull. Mutations affecting different functional domains of FGFR3 cause different forms of this lethal disorder.
[DISEASE] Defects in FGFR3 are a cause of craniosynostosis Adelaide type (CRSA) [MIM:600593]. CRSA is a form of coronal synostosis (CS) characterized by craniosynostosis, midface hypoplasia, downslanding palpebral fissures, ptosis, highly arched palate, mid-to-moderate sensorineural hearing loss, normal stature, bradydactyly and broad big toes. Radiologically, hands and feet show thimble-like middle phalanges, coned epiphyses, and carpal and tarsal fusions.
[DISEASE] Defects in FGFR3 are a cause of hypochondroplasia (HCH) [MIM:146000]. HCH is an autosomal dominant disease and is characterized by disproportionate short stature. It resembles achondroplasia, but with a less severe phenotype.
[DISEASE] Defects in FGFR3 are a cause of bladder cancer [MIM:109800]. Somatic mutations can constitutively activate FGFR3.
[DISEASE] Defects in FGFR3 are a cause of cervical cancer [MIM:603956].
[DISEASE] Involved in multiple myeloma (MM) through a chromosomal translocation t(4;14)(p16.3;q32.3) which invoves FGFR3 and the IgH locus (14q32).
[SIMILARITY] Belongs to the fibroblast growth factor receptor family.
[SIMILARITY] Contains 3 immunoglobulin-like C2-type domains.
[DATABASE] NAME=Atlas Genet. Cytogenet. Oncol. Haematol.; WWW='http://www.infobiogen.fr/services/chromcancer/Genes/FGFR99.html'.

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                     /note="K -> Q (in hypochondroplasia and bladder cancer; in
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1: NP_000133. fibroblast growth...[gi:4503711] BLink, Domains, Links

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LOCUS       NP_000133                 806 aa            linear   PRI 23-AUG-2004
DEFINITION  fibroblast growth factor receptor 3 isoform 1 precursor;
            hydroxyaryl-protein kinase; tyrosine kinase JTK4 [Homo sapiens].
ACCESSION   NP_000133
VERSION     NP_000133.1  GI:4503711
DBSOURCE    REFSEQ: accession NM_000142.2
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 806)
  AUTHORS   Trudel,S., Ely,S., Farooqi,Y., Affer,M., Robbiani,D.F., Chesi,M.
            and Bergsagel,P.L.
  TITLE     Inhibition of fibroblast growth factor receptor 3 induces
            differentiation and apoptosis in t(4;14) myeloma
  JOURNAL   Blood 103 (9), 3521-3528 (2004)
   PUBMED   14715624
  REMARK    GeneRIF: Inhibition of FGFR3 in myeloma cell lines was associated
            with morphologic, phenotypic, and functional changes typical of
            plasma cell differentiation, including increase in light-chain
            secretion and expression of CD31, followed by apoptosis
REFERENCE   2  (residues 1 to 806)
  AUTHORS   van Rhijn,B.W., van der Kwast,T.H., Vis,A.N., Kirkels,W.J.,
            Boeve,E.R., Jobsis,A.C. and Zwarthoff,E.C.
  TITLE     FGFR3 and P53 characterize alternative genetic pathways in the
            pathogenesis of urothelial cell carcinoma
  JOURNAL   Cancer Res. 64 (6), 1911-1914 (2004)
   PUBMED   15026322
  REMARK    GeneRIF: Mutations in growth factor receptor 3 is associated with
            the pathogenesis of urothelial cell carcinoma
REFERENCE   3  (residues 1 to 806)
  AUTHORS   Bakkar,A.A., Wallerand,H., Radvanyi,F., Lahaye,J.B., Pissard,S.,
            Lecerf,L., Kouyoumdjian,J.C., Abbou,C.C., Pairon,J.C.,
            Jaurand,M.C., Thiery,J.P., Chopin,D.K. and de Medina,S.G.
  TITLE     FGFR3 and TP53 gene mutations define two distinct pathways in
            urothelial cell carcinoma of the bladder
  JOURNAL   Cancer Res. 63 (23), 8108-8112 (2003)
   PUBMED   14678961
  REMARK    GeneRIF: FGFR3 mutations were associated with low-stage, low-grade
            urothelial carcinomas of the blader.
REFERENCE   4  (residues 1 to 806)
  AUTHORS   Dvorak,P., Dvorakova,D., Doubek,M., Faitova,J., Pacholikova,J.,
            Hampl,A. and Mayer,J.
  TITLE     Increased expression of fibroblast growth factor receptor 3 in
            CD34+ BCR-ABL+ cells from patients with chronic myeloid leukemia
  JOURNAL   Leukemia 17 (12), 2418-2425 (2003)
   PUBMED   14562121
  REMARK    GeneRIF: involvement of FGFR-3 in malignant hematopoiesis and
```

FGFR-3 tyrosine kinase in CD34+ leukemic cells
REFERENCE 5 (residues 1 to 806)
AUTHORS Koike,M., Yamanaka,Y., Inoue,M., Tanaka,H., Nishimura,R. and Seino,Y.
TITLE Insulin-like growth factor-1 rescues the mutated FGF receptor 3 (G380R) expressing ATDC5 cells from apoptosis through phosphatidylinositol 3-kinase and MAPK
JOURNAL J. Bone Miner. Res. 18 (11), 2043-2051 (2003)
PUBMED 14606518
REMARK GeneRIF: IGF-1 prevents the apoptosis induced by FGFR3 mutation through the PI3K pathway and MAPK pathway
REFERENCE 6 (residues 1 to 806)
AUTHORS Sturla,L.M., Merrick,A.E. and Burchill,S.A.
TITLE FGFR3IIIS: a novel soluble FGFR3 spliced variant that modulates growth is frequently expressed in tumour cells
JOURNAL Br. J. Cancer 89 (7), 1276-1284 (2003)
PUBMED 14520460
REMARK GeneRIF: FGFR3IIIS may regulate FGF and FGFR trafficking and function, possibly contributing to the development of a malignant phenotype
REFERENCE 7 (residues 1 to 806)
AUTHORS Yamanaka,Y., Tanaka,H., Koike,M., Nishimura,R. and Seino,Y.
TITLE PTHrP rescues ATDC5 cells from apoptosis induced by FGF receptor 3 mutation
JOURNAL J. Bone Miner. Res. 18 (8), 1395-1403 (2003)
PUBMED 12929929
REMARK GeneRIF: introduction of these mutated FGFR3s into ATDC5 cells downregulated PTHrP expression and induced apoptosis with reduction of Bcl-2 expression
REFERENCE 8 (residues 1 to 806)
AUTHORS Hyland,V.J., Robertson,S.P., Flanagan,S., Savarirayan,R., Roscioli,T., Masel,J., Hayes,M. and Glass,I.A.
TITLE Somatic and germline mosaicism for a R248C missense mutation in FGFR3, resulting in a skeletal dysplasia distinct from thanatophoric dysplasia
JOURNAL Am. J. Med. Genet. 120A (2), 157-168 (2003)
PUBMED 12833394
REMARK GeneRIF: A missense mutation in FGFR3 resulted in skeltal dysplasia distinct from thanatophoric dysplasia.
REFERENCE 9 (residues 1 to 806)
AUTHORS Lievens,P.M. and Liboi,E.
TITLE The thanatophoric dysplasia type II mutation hampers complete maturation of fibroblast growth factor receptor 3 (FGFR3), which activates signal transducer and activator of transcription 1 (STAT1) from the endoplasmic reticulum
JOURNAL J. Biol. Chem. 278 (19), 17344-17349 (2003)
PUBMED 12624096
REMARK GeneRIF: the importance of the immature FGFR3 proteins as mediators of an abnormal signaling in thanatophoric dysplasia type II
REFERENCE 10 (residues 1 to 806)
AUTHORS Reinhart,E., Eulert,S., Bill,J., Wurzler,K., Phan The,L. and Reuther,J.
TITLE Typical features of craniofacial growth of the FGFR3-associated coronal synostosis syndrome (so-called Muenke craniosynostosis)
JOURNAL Mund Kiefer Gesichtschir 7 (3), 132-137 (2003)
PUBMED 12764678
REMARK GeneRIF: The FGFR3-associated coronal synostosis syndrome (Muenke craniosynostosis) is caused by a point mutation (C749G) on the FGFR3 gene resulting in a Pro250Arg substitution.
REFERENCE 11 (residues 1 to 806)

AUTHORS Pehlivan,S., Ozkinay,F., Okutman,O., Cogulu,O., Ozcan,A., Cankaya,T. and Ulgenalp,A.
TITLE Achondroplasia in Turkey is defined by recurrent G380R mutation of the FGFR3 gene
JOURNAL Turk J Pediatr 45 (2), 99-101 (2003)
PUBMED 12921294
REMARK GeneRIF: results give further support to the fact that the G380R mutation of FGFR-3 is the most common mutation causing achondroplasia in different populations

REFERENCE 12 (residues 1 to 806)
AUTHORS Santra,M., Zhan,F., Tian,E., Barlogie,B. and Shaughnessy,J. Jr.
TITLE A subset of multiple myeloma harboring the t(4;14)(p16;q32) translocation lacks FGFR3 expression but maintains an IGH/MMSET fusion transcript
JOURNAL Blood 101 (6), 2374-2376 (2003)
PUBMED 12433679
REMARK GeneRIF: data indicate that t(4;14)(p16;q32) and loss of fibroblast growth factor receptor 3 occurred at a very early stage of multiple myeloma and suggest that activation of multiple myeloma SET domain protein may be transforming event of this translocation

REFERENCE 13 (residues 1 to 806)
AUTHORS Petschler,M., Stiller,M., Hoffmeister,B., Witkowski,R., Opitz,C., Bill,J.S. and Peters,H.
TITLE Clinical and molecular genetic observations on families with cherubism over three generations
JOURNAL Mund Kiefer Gesichtschir 7 (2), 83-87 (2003)
PUBMED 12664252
REMARK GeneRIF: Cherubism was mapped to region 4p16.3. Because of the associated craniosynostosis, we excluded the FGFR3 gene as a candidate gene for cherubism.

REFERENCE 14 (residues 1 to 806)
AUTHORS van Rhijn,B.W., van Tilborg,A.A., Lurkin,I., Bonaventure,J., de Vries,A., Thiery,J.P., van der Kwast,T.H., Zwarthoff,E.C. and Radvanyi,F.
TITLE Novel fibroblast growth factor receptor 3 (FGFR3) mutations in bladder cancer previously identified in non-lethal skeletal disorders
JOURNAL Eur. J. Hum. Genet. 10 (12), 819-824 (2002)
PUBMED 12461689
REMARK GeneRIF: mutations in bladder cancer previously identified in non-lethal skeletal disorders

REFERENCE 15 (residues 1 to 806)
AUTHORS Horton,W.A. and Lunstrum,G.P.
TITLE Fibroblast growth factor receptor 3 mutations in achondroplasia and related forms of dwarfism
JOURNAL Rev Endocr Metab Disord 3 (4), 381-385 (2002)
PUBMED 12424440
REMARK GeneRIF: strong correlation beween mutations of FGFR3 and disturbances of skeletal growth-REVIEW

REFERENCE 16 (residues 1 to 806)
AUTHORS Takenaka,H., Yasuno,H. and Kishimoto,S.
TITLE Immunolocalization of fibroblast growth factor receptors in normal and wounded human skin
JOURNAL Arch. Dermatol. Res. 294 (7), 331-338 (2002)
PUBMED 12373339
REMARK GeneRIF: Differences in spatial patterns of FGFR expression in normal skin may generate functional diversity in response to FGFs, and in wounded skin FGFs may function in wound healing via induced FGFRs.

REFERENCE 17 (residues 1 to 806)

AUTHORS Cormier,S., Delezoide,A.L., Benoist-Lasselin,C., Legeai-Mallet,L., Bonaventure,J. and Silve,C.
TITLE Parathyroid hormone receptor type 1/Indian hedgehog expression is preserved in the growth plate of human fetuses affected with fibroblast growth factor receptor type 3 activating mutations
JOURNAL Am. J. Pathol. 161 (4), 1325-1335 (2002)
PUBMED 12368206
REMARK GeneRIF: Parathyroid hormone receptor type 1/Indian hedgehog expression is preserved in the growth plate of human fetuses affected with activating mutations in this protein

REFERENCE 18 (residues 1 to 806)
AUTHORS Soverini,S., Terragna,C., Testoni,N., Ruggeri,D., Tosi,P., Zamagni,E., Cellini,C., Cavo,M., Baccarani,M., Tura,S. and Martinelli,G.
TITLE Novel mutation and RNA splice variant of fibroblast growth factor receptor 3 in multiple myeloma patients at diagnosis
JOURNAL Haematologica 87 (10), 1036-1040 (2002)
PUBMED 12368157
REMARK GeneRIF: there is an FGFR3 mutation with a demonstrated deregulatory mechanism and alternative splicing in the absence of t(4;14) in multiple myeloma patients

REFERENCE 19 (residues 1 to 806)
AUTHORS Monsonego-Ornan,E., Adar,R., Rom,E. and Yayon,A.
TITLE FGF receptors ubiquitylation: dependence on tyrosine kinase activity and role in downregulation
JOURNAL FEBS Lett. 528 (1-3), 83-89 (2002)
PUBMED 12297284
REMARK GeneRIF: phosphorylation is essential for FGFR3 ubiquitylation, but is not sufficient to induce downregulation of its internalization resistant mutants

REFERENCE 20 (residues 1 to 806)
AUTHORS Ni,J., Lu,G., Wang,W., Chen,F., Qin,H. and Wang,D.
TITLE Detection of fibroblast growth factor receptor 3 gene mutation at nucleotide 1138 site in congenita achondroplasia patients
JOURNAL Zhonghua Yi Xue Yi Chuan Xue Za Zhi 19 (3), 205-208 (2002)
PUBMED 12048679
REMARK GeneRIF: Nucleotide 1138 in transmembrane domain of FGFR3 gene is the hot point for mutation in ACH and hence its major pathologic cause.

REFERENCE 21 (residues 1 to 806)
AUTHORS Adar,R., Monsonego-Ornan,E., David,P. and Yayon,A.
TITLE Differential activation of cysteine-substitution mutants of fibroblast growth factor receptor 3 is determined by cysteine localization
JOURNAL J. Bone Miner. Res. 17 (5), 860-868 (2002)
PUBMED 12009017
REMARK GeneRIF: the G370C and S371C mutant receptors spontaneously dimerize in the correct spatial orientation required for effective signal transduction, whereas the 372-5 mutants, like the WT receptor, may achieve this orientation only on ligand binding

REFERENCE 22 (residues 1 to 806)
AUTHORS Jang,J.H.
TITLE Identification and characterization of soluble isoform of fibroblast growth factor receptor 3 in human SaOS-2 osteosarcoma cells
JOURNAL Biochem. Biophys. Res. Commun. 292 (2), 378-382 (2002)
PUBMED 11906172
REMARK GeneRIF: Identification and characterization of an alternatively spliced isoform

REFERENCE 23 (residues 1 to 806)

AUTHORS Camera,G., Baldi,M., Strisciuglio,G., Concolino,D., Mastroiacovo,P. and Baffico,M.
TITLE Occurrence of thanatophoric dysplasia type I (R248C) and hypochondroplasia (N540K) mutations in two patients with achondroplasia phenotype
JOURNAL Am. J. Med. Genet. 104 (4), 277-281 (2001)
PUBMED 11754059
REMARK GeneRIF: Two patients with clinical and radiological findings of achondroplasia, who had the most common FGFR3 missense mutations.
REFERENCE 24 (residues 1 to 806)
AUTHORS Yagasaki,F., Wakao,D., Yokoyama,Y., Uchida,Y., Murohashi,I., Kayano,H., Taniwaki,M., Matsuda,A. and Bessho,M.
TITLE Fusion of ETV6 to fibroblast growth factor receptor 3 in peripheral T-cell lymphoma with a t(4;12)(p16;p13) chromosomal translocation
JOURNAL Cancer Res. 61 (23), 8371-8374 (2001)
PUBMED 11731410
REMARK GeneRIF: We identified a novel ETV6 partner gene, fibroblast growth factor receptor 3 (FGFR3), in a patient with peripheral T-cell lymphoma (PTCL) with a t(4;12)(p16;p13) translocation.
REFERENCE 25 (residues 1 to 806)
AUTHORS La Rosa,S., Uccella,S., Erba,S., Capella,C. and Sessa,F.
TITLE Immunohistochemical detection of fibroblast growth factor receptors in normal endocrine cells and related tumors of the digestive system
JOURNAL Appl. Immunohistochem. Mol. Morphol. 9 (4), 319-328 (2001)
PUBMED 11759058
REMARK GeneRIF: distribution in normal endocrine cells and related tumors of the gastroenteropancreatic system; immunoreactive in duodenal G cells
REFERENCE 26 (residues 1 to 806)
AUTHORS Terada,M., Shimizu,A., Sato,N., Miyakaze,S.I., Katayama,H. and Kurokawa-Seo,M.
TITLE Fibroblast growth factor receptor 3 lacking the Ig IIIb and transmembrane domains secreted from human squamous cell carcinoma DJM-1 binds to FGFs
JOURNAL Mol. Cell Biol. Res. Commun. 4 (6), 365-373 (2001)
PUBMED 11703096
REFERENCE 27 (residues 1 to 806)
AUTHORS Shotelersuk,V., Ittiwut,C., Srivuthana,S., Wacharasindhu,S., Aroonparkmongkol,S., Mutirangura,A. and Poovorawan,Y.
TITLE Clinical and molecular characteristics of Thai patients with achondroplasia
JOURNAL Southeast Asian J. Trop. Med. Public Health 32 (2), 429-433 (2001)
PUBMED 11556601
REMARK GeneRIF: G380R mutation of this gene is common mutation associated with achondroplasia
REFERENCE 28 (residues 1 to 806)
AUTHORS Shimizu,A., Tada,K., Shukunami,C., Hiraki,Y., Kurokawa,T., Magane,N. and Kurokawa-Seo,M.
TITLE A novel alternatively spliced fibroblast growth factor receptor 3 isoform lacking the acid box domain is expressed during chondrogenic differentiation of ATDC5 cells
JOURNAL J. Biol. Chem. 276 (14), 11031-11040 (2001)
PUBMED 11134040
REFERENCE 29 (residues 1 to 806)
AUTHORS Hart,K.C., Robertson,S.C., Kanemitsu,M.Y., Meyer,A.N., Tynan,J.A. and Donoghue,D.J.
TITLE Transformation and Stat activation by derivatives of FGFR1, FGFR3, and FGFR4
JOURNAL Oncogene 19 (29), 3309-3320 (2000)

PUBMED 10918587
REFERENCE 30 (residues 1 to 806)
AUTHORS Passos-Bueno,M.R., Wilcox,W.R., Jabs,E.W., Sertie,A.L., Alonso,L.G. and Kitoh,H.
TITLE Clinical spectrum of fibroblast growth factor receptor mutations
JOURNAL Hum. Mutat. 14 (2), 115-125 (1999)
PUBMED 10425034
REFERENCE 31 (residues 1 to 806)
AUTHORS Perez-Castro,A.V., Wilson,J. and Altherr,M.R.
TITLE Genomic organization of the human fibroblast growth factor receptor 3 (FGFR3) gene and comparative sequence analysis with the mouse Fgfr3 gene
JOURNAL Genomics 41 (1), 10-16 (1997)
PUBMED 9126476
REFERENCE 32 (residues 1 to 806)
AUTHORS Deng,C., Wynshaw-Boris,A., Zhou,F., Kuo,A. and Leder,P.
TITLE Fibroblast growth factor receptor 3 is a negative regulator of bone growth
JOURNAL Cell 84 (6), 911-921 (1996)
PUBMED 8601314
REFERENCE 33 (residues 1 to 806)
AUTHORS Scotet,E. and Houssaint,E.
TITLE The choice between alternative IIIb and IIIc exons of the FGFR-3 gene is not strictly tissue-specific
JOURNAL Biochim. Biophys. Acta 1264 (2), 238-242 (1995)
PUBMED 7495869
REFERENCE 34 (residues 1 to 806)
AUTHORS Bellus,G.A., Hefferon,T.W., Ortiz de Luna,R.I., Hecht,J.T., Horton,W.A., Machado,M., Kaitila,I., McIntosh,I. and Francomano,C.A.
TITLE Achondroplasia is defined by recurrent G380R mutations of FGFR3
JOURNAL Am. J. Hum. Genet. 56 (2), 368-373 (1995)
PUBMED 7847369
REFERENCE 35 (residues 1 to 806)
AUTHORS Murgue,B., Tsunekawa,S., Rosenberg,I., deBeaumont,M. and Podolsky,D.K.
TITLE Identification of a novel variant form of fibroblast growth factor receptor 3 (FGFR3 IIIb) in human colonic epithelium
JOURNAL Cancer Res. 54 (19), 5206-5211 (1994)
PUBMED 7923141
REFERENCE 36 (residues 1 to 806)
AUTHORS Francomano,C.A., Ortiz de Luna,R.I., Hefferon,T.W., Bellus,G.A., Turner,C.E., Taylor,E., Meyers,D.A., Blanton,S.H., Murray,J.C., McIntosh,I. et al.
TITLE Localization of the achondroplasia gene to the distal 2.5 Mb of human chromosome 4p
JOURNAL Hum. Mol. Genet. 3 (5), 787-792 (1994)
PUBMED 8081365
REFERENCE 37 (residues 1 to 806)
AUTHORS Le Merrer,M., Rousseau,F., Legeai-Mallet,L., Landais,J.C., Pelet,A., Bonaventure,J., Sanak,M., Weissenbach,J., Stoll,C., Munnich,A. et al.
TITLE A gene for achondroplasia-hypochondroplasia maps to chromosome 4p
JOURNAL Nat. Genet. 6 (3), 318-321 (1994)
PUBMED 8012398
REFERENCE 38 (residues 1 to 806)
AUTHORS Velinov,M., Slaugenhaupt,S.A., Stoilov,I., Scott,C.I. Jr., Gusella,J.F. and Tsipouras,P.
TITLE The gene for achondroplasia maps to the telomeric region of chromosome 4p

JOURNAL Nat. Genet. 6 (3), 314-317 (1994)
PUBMED 8012397
REFERENCE 39 (residues 1 to 806)
AUTHORS Thompson,L.M., Plummer,S., Schalling,M., Altherr,M.R., Gusella,J.F., Housman,D.E. and Wasmuth,J.J.
TITLE A gene encoding a fibroblast growth factor receptor isolated from the Huntington disease gene region of human chromosome 4
JOURNAL Genomics 11 (4), 1133-1142 (1991)
PUBMED 1664411
REFERENCE 40 (residues 1 to 806)
AUTHORS Keegan,K., Johnson,D.E., Williams,L.T. and Hayman,M.J.
TITLE Isolation of an additional member of the fibroblast growth factor receptor family, FGFR-3
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 88 (4), 1095-1099 (1991)
PUBMED 1847508
REFERENCE 41 (residues 1 to 806)
AUTHORS Partanen,J., Makela,T.P., Alitalo,R., Lehvaslaiho,H. and Alitalo,K.
TITLE Putative tyrosine kinases expressed in K-562 human leukemia cells
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 87 (22), 8913-8917 (1990)
PUBMED 2247464
COMMENT REVIEWED REFSEQ: This record has been curated by NCBI staff. The reference sequence was derived from M58051.1 and M64347.1.

Summary: The protein encoded by this gene is a member of the fibroblast growth factor receptor family, where amino acid sequence is highly conserved between members and throughout evolution. FGFR family members differ from one another in their ligand affinities and tissue distribution. A full-length representative protein would consist of an extracellular region, composed of three immunoglobulin-like domains, a single hydrophobic membrane-spanning segment and a cytoplasmic tyrosine kinase domain. The extracellular portion of the protein interacts with fibroblast growth factors, setting in motion a cascade of downstream signals, ultimately influencing mitogenesis and differentiation. This particular family member binds acidic and basic fibroblast growth hormone and plays a role in bone development and maintenance. Mutations in this gene lead to craniosynostosis and multiple types of skeletal dysplasia. Alternative splicing occurs and additional variants have been described, including those utilizing alternate exon 8 rather than 9, but their full-length nature has not been determined.

Transcript Variant: This variant (1) is missing alternatively spliced exon 8 but utilizes alternatively spliced exon 9, resulting in isoform (1) with the IIIc-type C-terminal half of the IgIII domain.

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                     go_function: protein-tyrosine kinase activity [goid
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Sep 20 2004 06:46:12

1: NP_075254. fibroblast growth...[gi:13112048] BLink, Domains, Links

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DEFINITION  fibroblast growth factor receptor 3 isoform 2 precursor;
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ACCESSION   NP_075254
VERSION     NP_075254.1  GI:13112048
DBSOURCE    REFSEQ: accession NM_022965.1
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 694)
  AUTHORS   Trudel,S., Ely,S., Farooqi,Y., Affer,M., Robbiani,D.F., Chesi,M.
            and Bergsagel,P.L.
  TITLE     Inhibition of fibroblast growth factor receptor 3 induces
            differentiation and apoptosis in t(4;14) myeloma
  JOURNAL   Blood 103 (9), 3521-3528 (2004)
   PUBMED   14715624
  REMARK    GeneRIF: Inhibition of FGFR3 in myeloma cell lines was associated
            with morphologic, phenotypic, and functional changes typical of
            plasma cell differentiation, including increase in light-chain
            secretion and expression of CD31, followed by apoptosis
REFERENCE   2  (residues 1 to 694)
  AUTHORS   van Rhijn,B.W., van der Kwast,T.H., Vis,A.N., Kirkels,W.J.,
            Boeve,E.R., Jobsis,A.C. and Zwarthoff,E.C.
  TITLE     FGFR3 and P53 characterize alternative genetic pathways in the
            pathogenesis of urothelial cell carcinoma
  JOURNAL   Cancer Res. 64 (6), 1911-1914 (2004)
   PUBMED   15026322
  REMARK    GeneRIF: Mutations in growth factor receptor 3 is associated with
            the pathogenesis of urothelial cell carcinoma
REFERENCE   3  (residues 1 to 694)
  AUTHORS   Bakkar,A.A., Wallerand,H., Radvanyi,F., Lahaye,J.B., Pissard,S.,
            Lecerf,L., Kouyoumdjian,J.C., Abbou,C.C., Pairon,J.C.,
            Jaurand,M.C., Thiery,J.P., Chopin,D.K. and de Medina,S.G.
  TITLE     FGFR3 and TP53 gene mutations define two distinct pathways in
            urothelial cell carcinoma of the bladder
  JOURNAL   Cancer Res. 63 (23), 8108-8112 (2003)
   PUBMED   14678961
  REMARK    GeneRIF: FGFR3 mutations were associated with low-stage, low-grade
            urothelial carcinomas of the blader.
REFERENCE   4  (residues 1 to 694)
  AUTHORS   Dvorak,P., Dvorakova,D., Doubek,M., Faitova,J., Pacholikova,J.,
            Hampl,A. and Mayer,J.
  TITLE     Increased expression of fibroblast growth factor receptor 3 in
            CD34+ BCR-ABL+ cells from patients with chronic myeloid leukemia
  JOURNAL   Leukemia 17 (12), 2418-2425 (2003)
   PUBMED   14562121
  REMARK    GeneRIF: involvement of FGFR-3 in malignant hematopoiesis and
```

FGFR-3 tyrosine kinase in CD34+ leukemic cells
REFERENCE 5 (residues 1 to 694)
AUTHORS Koike,M., Yamanaka,Y., Inoue,M., Tanaka,H., Nishimura,R. and Seino,Y.
TITLE Insulin-like growth factor-1 rescues the mutated FGF receptor 3 (G380R) expressing ATDC5 cells from apoptosis through phosphatidylinositol 3-kinase and MAPK
JOURNAL J. Bone Miner. Res. 18 (11), 2043-2051 (2003)
PUBMED 14606518
REMARK GeneRIF: IGF-1 prevents the apoptosis induced by FGFR3 mutation through the PI3K pathway and MAPK pathway
REFERENCE 6 (residues 1 to 694)
AUTHORS Sturla,L.M., Merrick,A.E. and Burchill,S.A.
TITLE FGFR3IIIS: a novel soluble FGFR3 spliced variant that modulates growth is frequently expressed in tumour cells
JOURNAL Br. J. Cancer 89 (7), 1276-1284 (2003)
PUBMED 14520460
REMARK GeneRIF: FGFR3IIIS may regulate FGF and FGFR trafficking and function, possibly contributing to the development of a malignant phenotype
REFERENCE 7 (residues 1 to 694)
AUTHORS Yamanaka,Y., Tanaka,H., Koike,M., Nishimura,R. and Seino,Y.
TITLE PTHrP rescues ATDC5 cells from apoptosis induced by FGF receptor 3 mutation
JOURNAL J. Bone Miner. Res. 18 (8), 1395-1403 (2003)
PUBMED 12929929
REMARK GeneRIF: introduction of these mutated FGFR3s into ATDC5 cells downregulated PTHrP expression and induced apoptosis with reduction of Bcl-2 expression
REFERENCE 8 (residues 1 to 694)
AUTHORS Hyland,V.J., Robertson,S.P., Flanagan,S., Savarirayan,R., Roscioli,T., Masel,J., Hayes,M. and Glass,I.A.
TITLE Somatic and germline mosaicism for a R248C missense mutation in FGFR3, resulting in a skeletal dysplasia distinct from thanatophoric dysplasia
JOURNAL Am. J. Med. Genet. 120A (2), 157-168 (2003)
PUBMED 12833394
REMARK GeneRIF: A missense mutation in FGFR3 resulted in skeltal dysplasia distinct from thanatophoric dysplasia.
REFERENCE 9 (residues 1 to 694)
AUTHORS Lievens,P.M. and Liboi,E.
TITLE The thanatophoric dysplasia type II mutation hampers complete maturation of fibroblast growth factor receptor 3 (FGFR3), which activates signal transducer and activator of transcription 1 (STAT1) from the endoplasmic reticulum
JOURNAL J. Biol. Chem. 278 (19), 17344-17349 (2003)
PUBMED 12624096
REMARK GeneRIF: the importance of the immature FGFR3 proteins as mediators of an abnormal signaling in thanatophoric dysplasia type II
REFERENCE 10 (residues 1 to 694)
AUTHORS Reinhart,E., Eulert,S., Bill,J., Wurzler,K., Phan The,L. and Reuther,J.
TITLE Typical features of craniofacial growth of the FGFR3-associated coronal synostosis syndrome (so-called Muenke craniosynostosis)
JOURNAL Mund Kiefer Gesichtschir 7 (3), 132-137 (2003)
PUBMED 12764678
REMARK GeneRIF: The FGFR3-associated coronal synostosis syndrome (Muenke craniosynostosis) is caused by a point mutation (C749G) on the FGFR3 gene resulting in a Pro250Arg substitution.
REFERENCE 11 (residues 1 to 694)

AUTHORS Pehlivan,S., Ozkinay,F., Okutman,O., Cogulu,O., Ozcan,A., Cankaya,T. and Ulgenalp,A.
TITLE Achondroplasia in Turkey is defined by recurrent G380R mutation of the FGFR3 gene
JOURNAL Turk J Pediatr 45 (2), 99-101 (2003)
PUBMED 12921294
REMARK GeneRIF: results give further support to the fact that the G380R mutation of FGFR-3 is the most common mutation causing achondroplasia in different populations

REFERENCE 12 (residues 1 to 694)
AUTHORS Santra,M., Zhan,F., Tian,E., Barlogie,B. and Shaughnessy,J. Jr.
TITLE A subset of multiple myeloma harboring the t(4;14)(p16;q32) translocation lacks FGFR3 expression but maintains an IGH/MMSET fusion transcript
JOURNAL Blood 101 (6), 2374-2376 (2003)
PUBMED 12433679
REMARK GeneRIF: data indicate that t(4;14)(p16;q32) and loss of fibroblast growth factor receptor 3 occurred at a very early stage of multiple myeloma and suggest that activation of multiple myeloma SET domain protein may be transforming event of this translocation

REFERENCE 13 (residues 1 to 694)
AUTHORS Petschler,M., Stiller,M., Hoffmeister,B., Witkowski,R., Opitz,C., Bill,J.S. and Peters,H.
TITLE Clinical and molecular genetic observations on families with cherubism over three generations
JOURNAL Mund Kiefer Gesichtschir 7 (2), 83-87 (2003)
PUBMED 12664252
REMARK GeneRIF: Cherubism was mapped to region 4p16.3. Because of the associated craniosynostosis, we excluded the FGFR3 gene as a candidate gene for cherubism.

REFERENCE 14 (residues 1 to 694)
AUTHORS van Rhijn,B.W., van Tilborg,A.A., Lurkin,I., Bonaventure,J., de Vries,A., Thiery,J.P., van der Kwast,T.H., Zwarthoff,E.C. and Radvanyi,F.
TITLE Novel fibroblast growth factor receptor 3 (FGFR3) mutations in bladder cancer previously identified in non-lethal skeletal disorders
JOURNAL Eur. J. Hum. Genet. 10 (12), 819-824 (2002)
PUBMED 12461689
REMARK GeneRIF: mutations in bladder cancer previously identified in non-lethal skeletal disorders

REFERENCE 15 (residues 1 to 694)
AUTHORS Horton,W.A. and Lunstrum,G.P.
TITLE Fibroblast growth factor receptor 3 mutations in achondroplasia and related forms of dwarfism
JOURNAL Rev Endocr Metab Disord 3 (4), 381-385 (2002)
PUBMED 12424440
REMARK GeneRIF: strong correlation beween mutations of FGFR3 and disturbances of skeletal growth-REVIEW

REFERENCE 16 (residues 1 to 694)
AUTHORS Takenaka,H., Yasuno,H. and Kishimoto,S.
TITLE Immunolocalization of fibroblast growth factor receptors in normal and wounded human skin
JOURNAL Arch. Dermatol. Res. 294 (7), 331-338 (2002)
PUBMED 12373339
REMARK GeneRIF: Differences in spatial patterns of FGFR expression in normal skin may generate functional diversity in response to FGFs, and in wounded skin FGFs may function in wound healing via induced FGFRs.

REFERENCE 17 (residues 1 to 694)

AUTHORS Cormier,S., Delezoide,A.L., Benoist-Lasselin,C., Legeai-Mallet,L., Bonaventure,J. and Silve,C.
TITLE Parathyroid hormone receptor type 1/Indian hedgehog expression is preserved in the growth plate of human fetuses affected with fibroblast growth factor receptor type 3 activating mutations
JOURNAL Am. J. Pathol. 161 (4), 1325-1335 (2002)
PUBMED 12368206
REMARK GeneRIF: Parathyroid hormone receptor type 1/Indian hedgehog expression is preserved in the growth plate of human fetuses affected with activating mutations in this protein

REFERENCE 18 (residues 1 to 694)
AUTHORS Soverini,S., Terragna,C., Testoni,N., Ruggeri,D., Tosi,P., Zamagni,E., Cellini,C., Cavo,M., Baccarani,M., Tura,S. and Martinelli,G.
TITLE Novel mutation and RNA splice variant of fibroblast growth factor receptor 3 in multiple myeloma patients at diagnosis
JOURNAL Haematologica 87 (10), 1036-1040 (2002)
PUBMED 12368157
REMARK GeneRIF: there is an FGFR3 mutation with a demonstrated deregulatory mechanism and alternative splicing in the absence of t(4;14) in multiple myeloma patients

REFERENCE 19 (residues 1 to 694)
AUTHORS Monsonego-Ornan,E., Adar,R., Rom,E. and Yayon,A.
TITLE FGF receptors ubiquitylation: dependence on tyrosine kinase activity and role in downregulation
JOURNAL FEBS Lett. 528 (1-3), 83-89 (2002)
PUBMED 12297284
REMARK GeneRIF: phosphorylation is essential for FGFR3 ubiquitylation, but is not sufficient to induce downregulation of its internalization resistant mutants

REFERENCE 20 (residues 1 to 694)
AUTHORS Ni,J., Lu,G., Wang,W., Chen,F., Qin,H. and Wang,D.
TITLE Detection of fibroblast growth factor receptor 3 gene mutation at nucleotide 1138 site in congenita achondroplasia patients
JOURNAL Zhonghua Yi Xue Yi Chuan Xue Za Zhi 19 (3), 205-208 (2002)
PUBMED 12048679
REMARK GeneRIF: Nucleotide 1138 in transmembrane domain of FGFR3 gene is the hot point for mutation in ACH and hence its major pathologic cause.

REFERENCE 21 (residues 1 to 694)
AUTHORS Adar,R., Monsonego-Ornan,E., David,P. and Yayon,A.
TITLE Differential activation of cysteine-substitution mutants of fibroblast growth factor receptor 3 is determined by cysteine localization
JOURNAL J. Bone Miner. Res. 17 (5), 860-868 (2002)
PUBMED 12009017
REMARK GeneRIF: the G370C and S371C mutant receptors spontaneously dimerize in the correct spatial orientation required for effective signal transduction, whereas the 372-5 mutants, like the WT receptor, may achieve this orientation only on ligand binding

REFERENCE 22 (residues 1 to 694)
AUTHORS Jang,J.H.
TITLE Identification and characterization of soluble isoform of fibroblast growth factor receptor 3 in human SaOS-2 osteosarcoma cells
JOURNAL Biochem. Biophys. Res. Commun. 292 (2), 378-382 (2002)
PUBMED 11906172
REMARK GeneRIF: Identification and characterization of an alternatively spliced isoform

REFERENCE 23 (residues 1 to 694)

AUTHORS Camera,G., Baldi,M., Strisciuglio,G., Concolino,D., Mastroiacovo,P. and Baffico,M.
TITLE Occurrence of thanatophoric dysplasia type I (R248C) and hypochondroplasia (N540K) mutations in two patients with achondroplasia phenotype
JOURNAL Am. J. Med. Genet. 104 (4), 277-281 (2001)
PUBMED 11754059
REMARK GeneRIF: Two patients with clinical and radiological findings of achondroplasia, who had the most common FGFR3 missense mutations.
REFERENCE 24 (residues 1 to 694)
AUTHORS Yagasaki,F., Wakao,D., Yokoyama,Y., Uchida,Y., Murohashi,I., Kayano,H., Taniwaki,M., Matsuda,A. and Bessho,M.
TITLE Fusion of ETV6 to fibroblast growth factor receptor 3 in peripheral T-cell lymphoma with a t(4;12)(p16;p13) chromosomal translocation
JOURNAL Cancer Res. 61 (23), 8371-8374 (2001)
PUBMED 11731410
REMARK GeneRIF: We identified a novel ETV6 partner gene, fibroblast growth factor receptor 3 (FGFR3), in a patient with peripheral T-cell lymphoma (PTCL) with a t(4;12)(p16;p13) translocation.
REFERENCE 25 (residues 1 to 694)
AUTHORS La Rosa,S., Uccella,S., Erba,S., Capella,C. and Sessa,F.
TITLE Immunohistochemical detection of fibroblast growth factor receptors in normal endocrine cells and related tumors of the digestive system
JOURNAL Appl. Immunohistochem. Mol. Morphol. 9 (4), 319-328 (2001)
PUBMED 11759058
REMARK GeneRIF: distribution in normal endocrine cells and related tumors of the gastroenteropancreatic system; immunoreactive in duodenal G cells
REFERENCE 26 (residues 1 to 694)
AUTHORS Terada,M., Shimizu,A., Sato,N., Miyakaze,S.I., Katayama,H. and Kurokawa-Seo,M.
TITLE Fibroblast growth factor receptor 3 lacking the Ig IIIb and transmembrane domains secreted from human squamous cell carcinoma DJM-1 binds to FGFs
JOURNAL Mol. Cell Biol. Res. Commun. 4 (6), 365-373 (2001)
PUBMED 11703096
REFERENCE 27 (residues 1 to 694)
AUTHORS Shotelersuk,V., Ittiwut,C., Srivuthana,S., Wacharasindhu,S., Aroonparkmongkol,S., Mutirangura,A. and Poovorawan,Y.
TITLE Clinical and molecular characteristics of Thai patients with achondroplasia
JOURNAL Southeast Asian J. Trop. Med. Public Health 32 (2), 429-433 (2001)
PUBMED 11556601
REMARK GeneRIF: G380R mutation of this gene is common mutation associated with achondroplasia
REFERENCE 28 (residues 1 to 694)
AUTHORS Shimizu,A., Tada,K., Shukunami,C., Hiraki,Y., Kurokawa,T., Magane,N. and Kurokawa-Seo,M.
TITLE A novel alternatively spliced fibroblast growth factor receptor 3 isoform lacking the acid box domain is expressed during chondrogenic differentiation of ATDC5 cells
JOURNAL J. Biol. Chem. 276 (14), 11031-11040 (2001)
PUBMED 11134040
REFERENCE 29 (residues 1 to 694)
AUTHORS Hart,K.C., Robertson,S.C., Kanemitsu,M.Y., Meyer,A.N., Tynan,J.A. and Donoghue,D.J.
TITLE Transformation and Stat activation by derivatives of FGFR1, FGFR3, and FGFR4
JOURNAL Oncogene 19 (29), 3309-3320 (2000)

PUBMED 10918587
REFERENCE 30 (residues 1 to 694)
AUTHORS Passos-Bueno,M.R., Wilcox,W.R., Jabs,E.W., Sertie,A.L., Alonso,L.G. and Kitoh,H.
TITLE Clinical spectrum of fibroblast growth factor receptor mutations
JOURNAL Hum. Mutat. 14 (2), 115-125 (1999)
PUBMED 10425034
REFERENCE 31 (residues 1 to 694)
AUTHORS Perez-Castro,A.V., Wilson,J. and Altherr,M.R.
TITLE Genomic organization of the human fibroblast growth factor receptor 3 (FGFR3) gene and comparative sequence analysis with the mouse Fgfr3 gene
JOURNAL Genomics 41 (1), 10-16 (1997)
PUBMED 9126476
REFERENCE 32 (residues 1 to 694)
AUTHORS Deng,C., Wynshaw-Boris,A., Zhou,F., Kuo,A. and Leder,P.
TITLE Fibroblast growth factor receptor 3 is a negative regulator of bone growth
JOURNAL Cell 84 (6), 911-921 (1996)
PUBMED 8601314
REFERENCE 33 (residues 1 to 694)
AUTHORS Scotet,E. and Houssaint,E.
TITLE The choice between alternative IIIb and IIIc exons of the FGFR-3 gene is not strictly tissue-specific
JOURNAL Biochim. Biophys. Acta 1264 (2), 238-242 (1995)
PUBMED 7495869
REFERENCE 34 (residues 1 to 694)
AUTHORS Bellus,G.A., Hefferon,T.W., Ortiz de Luna,R.I., Hecht,J.T., Horton,W.A., Machado,M., Kaitila,I., McIntosh,I. and Francomano,C.A.
TITLE Achondroplasia is defined by recurrent G380R mutations of FGFR3
JOURNAL Am. J. Hum. Genet. 56 (2), 368-373 (1995)
PUBMED 7847369
REFERENCE 35 (residues 1 to 694)
AUTHORS Murgue,B., Tsunekawa,S., Rosenberg,I., deBeaumont,M. and Podolsky,D.K.
TITLE Identification of a novel variant form of fibroblast growth factor receptor 3 (FGFR3 IIIb) in human colonic epithelium
JOURNAL Cancer Res. 54 (19), 5206-5211 (1994)
PUBMED 7923141
REFERENCE 36 (residues 1 to 694)
AUTHORS Francomano,C.A., Ortiz de Luna,R.I., Hefferon,T.W., Bellus,G.A., Turner,C.E., Taylor,E., Meyers,D.A., Blanton,S.H., Murray,J.C., McIntosh,I. et al.
TITLE Localization of the achondroplasia gene to the distal 2.5 Mb of human chromosome 4p
JOURNAL Hum. Mol. Genet. 3 (5), 787-792 (1994)
PUBMED 8081365
REFERENCE 37 (residues 1 to 694)
AUTHORS Le Merrer,M., Rousseau,F., Legeai-Mallet,L., Landais,J.C., Pelet,A., Bonaventure,J., Sanak,M., Weissenbach,J., Stoll,C., Munnich,A. et al.
TITLE A gene for achondroplasia-hypochondroplasia maps to chromosome 4p
JOURNAL Nat. Genet. 6 (3), 318-321 (1994)
PUBMED 8012398
REFERENCE 38 (residues 1 to 694)
AUTHORS Velinov,M., Slaugenhaupt,S.A., Stoilov,I., Scott,C.I. Jr., Gusella,J.F. and Tsipouras,P.
TITLE The gene for achondroplasia maps to the telomeric region of chromosome 4p

JOURNAL Nat. Genet. 6 (3), 314-317 (1994)
PUBMED 8012397
REFERENCE 39 (residues 1 to 694)
AUTHORS Thompson,L.M., Plummer,S., Schalling,M., Altherr,M.R., Gusella,J.F., Housman,D.E. and Wasmuth,J.J.
TITLE A gene encoding a fibroblast growth factor receptor isolated from the Huntington disease gene region of human chromosome 4
JOURNAL Genomics 11 (4), 1133-1142 (1991)
PUBMED 1664411
REFERENCE 40 (residues 1 to 694)
AUTHORS Keegan,K., Johnson,D.E., Williams,L.T. and Hayman,M.J.
TITLE Isolation of an additional member of the fibroblast growth factor receptor family, FGFR-3
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 88 (4), 1095-1099 (1991)
PUBMED 1847508
REFERENCE 41 (residues 1 to 694)
AUTHORS Partanen,J., Makela,T.P., Alitalo,R., Lehvaslaiho,H. and Alitalo,K.
TITLE Putative tyrosine kinases expressed in K-562 human leukemia cells
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 87 (22), 8913-8917 (1990)
PUBMED 2247464
COMMENT REVIEWED REFSEQ: This record has been curated by NCBI staff. The reference sequence was derived from AF245114.1 and M64347.1.

Summary: The protein encoded by this gene is a member of the fibroblast growth factor receptor family, where amino acid sequence is highly conserved between members and throughout evolution. FGFR family members differ from one another in their ligand affinities and tissue distribution. A full-length representative protein would consist of an extracellular region, composed of three immunoglobulin-like domains, a single hydrophobic membrane-spanning segment and a cytoplasmic tyrosine kinase domain. The extracellular portion of the protein interacts with fibroblast growth factors, setting in motion a cascade of downstream signals, ultimately influencing mitogenesis and differentiation. This particular family member binds acidic and basic fibroblast growth hormone and plays a role in bone development and maintenance. Mutations in this gene lead to craniosynostosis and multiple types of skeletal dysplasia. Alternative splicing occurs and additional variants have been described, including those utilizing alternate exon 8 rather than 9, but their full-length nature has not been determined.

Transcript Variant: This variant (2) does not contain alternatively spliced exons 8 or 9, resulting in a loss of the C-terminal half of the IgIII domain. In addition, this variant is missing alternatively spliced exon 10 which encodes the transmembrane region, suggesting a soluble receptor.

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